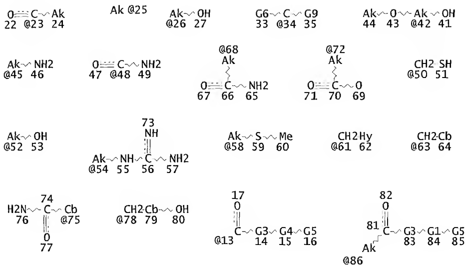
Attempt to cover claim 1 | packet #1

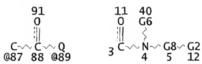
Claim 1 is really broad. I did a number of iterations but there are still a lot of cpds. I limited by crossing w/ melanin & di- or tripeptide & date. see p7 the cpds in the cites aren't great. I labeled the cpds as good or bad.

I decided to search claim 2. See packet #2

=> d que 191
L18 STR



Page 1-A



Page 2-A

```
REP G1=(0-1) 87-83 89-85
VAR G2=86/13
VAR G3=N/O
REP G4=(0-1) 87-14 89-16
VAR G5=H/23/25/26/42
VAR G6=H/25
VAR G8=CH2/34
VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  25
CONNECT IS E2  RC AT  26
CONNECT IS E2  RC AT  42
CONNECT IS E1  RC AT  44
CONNECT IS E2  RC AT  54
CONNECT IS E2  RC AT  58
CONNECT IS E1  RC AT  62
CONNECT IS E1  RC AT  64
CONNECT IS E2  RC AT  68
CONNECT IS E1  RC AT  69
CONNECT IS E2  RC AT  72
CONNECT IS E2  RC AT  75
CONNECT IS E2  RC AT  79
CONNECT IS E2  RC AT  86
DEFAULT MLEVEL IS ATOM
GGCAT   IS UNS  AT  62
GGCAT   IS MCY  UNS  AT  64
GGCAT   IS MCY  UNS  AT  75
GGCAT   IS MCY  UNS  AT  79
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X3 C  AT  42
ECOUNT  IS X2 C  AT  52
ECOUNT  IS E2 C  AT  58
```

```
ECOUNT  IS M3-X8 C  X2 N  AT  62
ECOUNT  IS E6 C  AT  64
ECOUNT  IS X2 C  AT  68
ECOUNT  IS X2 C  AT  72
ECOUNT  IS E6 C  AT  75
ECOUNT  IS E6 C  AT  79

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  70

STEREO ATTRIBUTES: NONE
L40              STR
```


```
REP G1=(0-7) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS PCY  UNS  AT   1
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E10 C  AT   1

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   6

STEREO ATTRIBUTES: NONE
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L42 (      32652)SEA FILE=REGISTRY SUB=L41 SSS FUL L40
L43              STR
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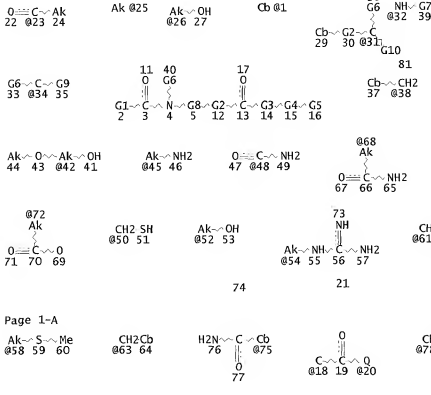

Page 1-A

```
Page 2-A
VAR G1=1/31/38
REP G2=(0-6) C
VAR G3=N/O
REP G4=(0-1) 18-14 20-16
VAR G5=H/23/25/26/42
VAR G6=H/25
VAR G7=23/25/26/42
VAR G8=CH2/34
VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78
VAR G10=NH2/32
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  24
CONNECT IS E1  RC AT  25
CONNECT IS E2  RC AT  26
CONNECT IS E2  RC AT  42
CONNECT IS E1  RC AT  44
CONNECT IS E2  RC AT  54
CONNECT IS E2  RC AT  58
CONNECT IS E1  RC AT  62
CONNECT IS E1  RC AT  64
CONNECT IS E2  RC AT  68
CONNECT IS E1  RC AT  69
CONNECT IS E2  RC AT  72
CONNECT IS E2  RC AT  75
CONNECT IS E2  RC AT  79
DEFAULT MLEVEL IS ATOM
GGCAT   IS PCY  UNS  AT   1
GGCAT   IS PCY  UNS  AT  29
GGCAT   IS PCY  UNS  AT  37
GGCAT   IS UNS  AT  62
GGCAT   IS MCY  UNS  AT  64
GGCAT   IS MCY  UNS  AT  75
GGCAT   IS MCY  UNS  AT  79
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E10 C  AT   1
ECOUNT  IS E10 C  AT  29
ECOUNT  IS E10 C  AT  37
ECOUNT  IS X3 C  AT  42
ECOUNT  IS X2 C  AT  52
ECOUNT  IS E2 C  AT  58
ECOUNT  IS M3-X8 C  X2 N  AT  62
ECOUNT  IS E6 C  AT  64
ECOUNT  IS X2 C  AT  68
ECOUNT  IS X2 C  AT  72
ECOUNT  IS E6 C  AT  75
ECOUNT  IS E6 C  AT  79

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  75

STEREO ATTRIBUTES: NONE
L44 (       3196)SEA FILE=REGISTRY SUB=L42 SSS FUL L43
L45         2873 SEA FILE=REGISTRY ABB=ON  PLU=ON  L44/COM
L46         2701 SEA FILE=REGISTRY SUB=L45 SSS FUL L18
L53              STR
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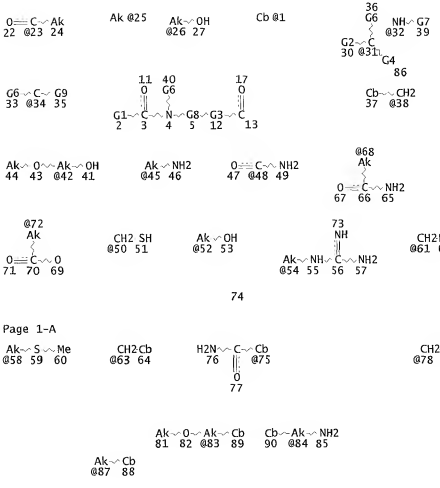

Page 1-A

Page 2-A
VAR G1=1/31/38
VAR G2=1/87/83/84
REP G3=(0-6) C
VAR G4=NH2/32
VAR G6=H/25
VAR G7=23/25/26/42
VAR G8=CH2/34
VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 1
CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 25
CONNECT IS E2 RC AT 26
CONNECT IS E1 RC AT 37
CONNECT IS E3 RC AT 42
CONNECT IS E1 RC AT 44
CONNECT IS E2 RC AT 45
CONNECT IS E2 RC AT 54
CONNECT IS E2 RC AT 58
CONNECT IS E1 RC AT 62
CONNECT IS E1 RC AT 64
CONNECT IS E2 RC AT 68
CONNECT IS E1 RC AT 69
CONNECT IS E2 RC AT 72
CONNECT IS E2 RC AT 75

```
CONNECT IS E2  RC AT  79
CONNECT IS E1  RC AT  81
CONNECT IS E2  RC AT  87
DEFAULT MLEVEL IS ATOM
GGCAT   IS PCY  UNS  AT   1
GGCAT   IS PCY  UNS  AT  37
GGCAT   IS UNS  AT  62
GGCAT   IS MCY  UNS  AT  64
GGCAT   IS MCY  UNS  AT  75
GGCAT   IS MCY  UNS  AT  79
GGCAT   IS PCY  UNS  AT  88
GGCAT   IS PCY  UNS  AT  89
GGCAT   IS PCY  UNS  AT  90
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E10 C  AT   1
ECOUNT  IS E10 C  AT  37
ECOUNT  IS X3 C  AT  42
ECOUNT  IS X2 C  AT  52
ECOUNT  IS E2 C  AT  58
ECOUNT  IS M3-X8 C  X2 N  AT  62
ECOUNT  IS E6 C  AT  64
ECOUNT  IS X2 C  AT  68
ECOUNT  IS X2 C  AT  72
ECOUNT  IS E6 C  AT  75
ECOUNT  IS E6 C  AT  79
ECOUNT  IS E10 C  AT  88
ECOUNT  IS E10 C  AT  89
ECOUNT  IS E10 C  AT  90

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  76

STEREO ATTRIBUTES: NONE
L54         1894 SEA FILE=REGISTRY SUB=L45 SSS FUL L53
L56         1782 SEA FILE=REGISTRY ABB=ON  PLU=ON  L54 AND L46
L58         1704 SEA FILE=REGISTRY ABB=ON  PLU=ON  L56 NOT ((C N S) OR CO OR C
                 N O OR C S)/RELF
L59         1551 SEA FILE=REGISTRY ABB=ON  PLU=ON  L58 NOT (M/ELS OR B/ELS OR
                 SI/ELS OR NC5/ESS OR N2C3/ES OR "NITRO" OR "HYDROXYAMINO")
L61         1405 SEA FILE=REGISTRY ABB=ON  PLU=ON  L59 AND 1 591.49.57/RID
L62         1383 SEA FILE=REGISTRY ABB=ON  PLU=ON  L61 NOT ("FLUOREN" OR
                 "TRICYCLO")
L63         1259 SEA FILE=REGISTRY ABB=ON  PLU=ON  L62 NOT X/ELS
L64         1234 SEA FILE=REGISTRY ABB=ON  PLU=ON  L63 AND NC=1 NOT NC6/ESS
L68         1202 SEA FILE=REGISTRY ABB=ON  PLU=ON  L64 NOT (P/ELS OR OCS/ES)
L76              STR
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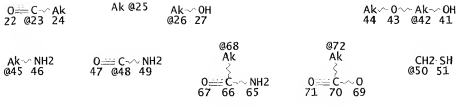
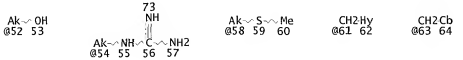
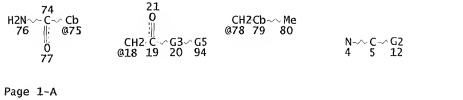
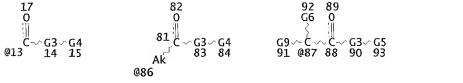






Page 1-A



Page 2-A
VAR G2=13/86
VAR G3=NH/O
VAR G4=H/23/25/26/42/87/18
VAR G5=H/23/25/26/42
VAR G6=H/25
VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 24
CONNECT IS E1 RC AT 25
CONNECT IS E2 RC AT 26
CONNECT IS E3 RC AT 42
CONNECT IS E1 RC AT 44
CONNECT IS E2 RC AT 54
CONNECT IS E2 RC AT 58
CONNECT IS E1 RC AT 62
CONNECT IS E1 RC AT 64
CONNECT IS E2 RC AT 68
CONNECT IS E1 RC AT 69
CONNECT IS E2 RC AT 72
CONNECT IS E2 RC AT 75
CONNECT IS E2 RC AT 79
CONNECT IS E2 RC AT 86
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 62
GGCAT IS MCY UNS AT 64
GGCAT IS MCY UNS AT 75
GGCAT IS MCY UNS AT 79
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS X3 C AT 42
ECOUNT IS X2 C AT 52
ECOUNT IS E2 C AT 58
ECOUNT IS M3-X8 C X2 N AT 62
ECOUNT IS E6 C AT 64
ECOUNT IS X2 C AT 68

```
ECOUNT  IS X2 C  AT  72
ECOUNT  IS E6 C  AT  75
ECOUNT  IS E6 C  AT  79

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  70

STEREO ATTRIBUTES: NONE
L78        1182 SEA FILE=REGISTRY SUB=L68 SSS FUL L76
L85        1094 SEA FILE=REGISTRY ABB=ON  PLU=ON  L78 NOT ("FURAN" OR "PYRROLID
                INYL" OR C O/RELF)
L86        1037 SEA FILE=REGISTRY ABB=ON  PLU=ON  L85 NOT ("BENZODIAZEPIN" OR
                "NITRILE" OR "CYANO" OR "FORMYL")
L87         425 SEA FILE=CAPLUS ABB=ON  PLU=ON  L86
L88           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L87 AND ?MELAN?
L89          28 SEA FILE=CAPLUS ABB=ON  PLU=ON  L87 AND (DIPEPTIDE OR TRIPEPTID
                E)/OBI
L90          35 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L88 OR L89)
L91          25 SEA FILE=CAPLUS ABB=ON  PLU=ON  L90 AND PY<2001
```

← use

← limited by data

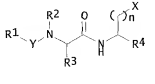
=> d ibib abs hitstr 1-10

L91 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:312019 CAPLUS
DOCUMENT NUMBER: 136:325828
TITLE: Preparation of **dipeptide** derivatives as cell adhesion inhibitors
INVENTOR(S): Adams, Steven P.; Lin, Ko-Chung; Lee, Wen-Cherng; Castro, Alfredo C.; Zimmerman, Craig N.; Hammond, Charles E.; Liao, Yu-Sheng; Cuervo, Julio Hernan; Singh, Juswinder
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: U.S., 50 pp., Cont.-in-part of U.S. 6,306,840.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

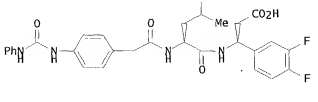
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6376538	B1	20020423	US 1997-875321	19970919
US 6306840	B1	20011023	US 1995-376372	19950123
WO 9622966	A1	19960801	WO 1996-US1349	19960118 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
EP 1142867	A2	20011010	EP 2001-107877	19960118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
US 2003018016	A1	20030123	US 2001-2341	20011023

PRIORITY APPLN. INFO.: US 1995-376372 A2 19950123
WO 1996-US1349 W 19960118
EP 1996-905316 A3 19960118
US 1997-875321 A3 19970919

OTHER SOURCE(S): MARPAT 136:325828
GI



I



II

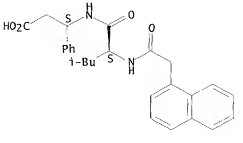
AB Novel dipeptide analogs I [X = CO2H, PO3H-, SO2R5, SO3H, OPO3H-, CO2R4; Y = CO, SO2, PO2; n = 0-2; R1 = optionally substituted alkyl, alkenyl, alkynyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl, alkoxy, alkenyloxy, aralkoxy, alkylamino, alkenylamino,

alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, heterocyclyl; R2 = H, aryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aralkyl; R2NCR3 = heterocyclic ring; R3 = natural, unnatural, modified, or substituted amino acid side chain; R4 = optionally substituted aryl, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aralkyl, H, heterocyclyl, heterocyclylcarbonyl, aminocarbonyl, amido, alkylaminocarbonyl, arylaminocarbonyl, acylaminocarbonyl, acyl; R5 = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl] are prepd. as compds. useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical compns. of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, .beta.-amino acid-contg. dipeptide II, prepd. by std. methods, displayed an IC50 of <50 nM in a cell adhesion inhibition assay.

IT **181520-01-4P 181520-03-6P 181520-87-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .beta.-amino acid **dipeptide** derivs. as cell adhesion inhibitors)

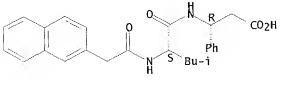
RN 181520-01-4 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(1-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



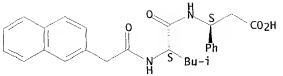
RN 181520-03-6 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



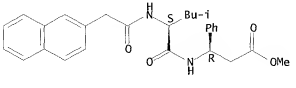
RN 181520-87-6 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



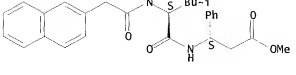
IT **181518-17-2P 181518-19-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .beta.-amino acid **dipeptide** derivs. as cell adhesion inhibitors)
RN 181518-17-2 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 181518-19-4 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:366736 CAPLUS
DOCUMENT NUMBER: 134:340711
TITLE: Preparation of **tripeptide** .alpha.-ketoamides as serine and cysteine protease inhibitors
INVENTOR(S): Powers, James C.
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. 5,650,508.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6235929	B1	20010522	US 1996-777354	19961227
US 5650508	A	19970722	US 1995-539944	19951006 <--
PRIORITY APPLN. INFO.:			US 1991-815073 B1	19911227
			US 1993-118997 B1	19930909

US 1994-246511 B1 19940520
US 1995-539944 A2 19951006

OTHER SOURCE(S): MARPAT 134:340711
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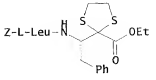


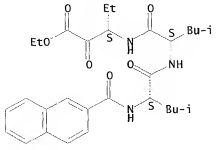
I

AB Tripeptide .alpha.-ketoamides M1-AA1-AA2-AA3-CONR3R4 [M1 = H, NH2CO, NH2CS, NH2SO2, XNHCO, X2NCO, XNHCS, X2NCS, XNHSO2, X2NSO2, XCO, XCS, XSO2, XO2C, XOCS; X = (un)substituted C1-10 alkyl or fluoroalkyl, 1-adamantyl, 9-fluorenyl, (un)substituted Ph or naphthyl; AA1 and AA2 = independently side-chain (un)blocked amino acid selected from alanine, valine, leucine, isoleucine, glycine, serine, aspartic acid, and glutamic acid; AA3 = aspartic or glutamic acid; R3 = alkyl or cycloalkyl substituted by Ph and optionally other substituents; R4 = H, alkyl or cycloalkyl which may have a Ph group and other substituents] were prepd. as serine and cysteine protease inhibitors. Thus, condensation of protected peptidyl ketoester I (Z = PhCH2O2C) (prepd. in 3 steps from Z-Leu-Phe-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH2 (R = Et, Pr, Bu, Bu-i, CH2Ph, CH2CH2Ph) gave peptidyl ketoamides Z-Leu-Phe-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with Ki = 8-73 .mu.M and had half-lives in liver and plasma of >60.

IT **170902-24-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of peptide ketoamides as serine and cysteine protease inhibitors)

RN 170902-24-6 CAPLUS
CN L-Leucinamide, N-(2-naphthalenylcarbonyl)-L-leucyl-N-[(1S)-3-ethoxy-1-ethyl-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:772657 CAPLUS
DOCUMENT NUMBER: 133:329599
TITLE: **Melanocyte**-stimulating hormone inhibitors
INVENTOR(S): Shiojiri, Eiji; Takino, Yoshinobu; Chujou, Hiromi; Sakamoto, Kazutami; Ijichi, Chiori; Eto, Yuzuru; Iwasaki, Keiji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 37 pp.

applicant

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064926	A1	20001102	WO 2000-JP2687	20000425 <--
W: CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1174437	A1	20020123	EP 2000-917447	20000425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1999-118633 A 19990426
WO 2000-JP2687 W 20000425

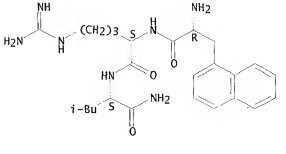
AB MSH inhibitors characterized by contg., as the active ingredient, di- or tripeptide derivs. having a specific naphthyl group or salts thereof, or a MSH inhibiting compd. showing a 50% inhibitory concn. (IC50) on cAMP prodn. of 100 nm or less. These inhibitors can inhibit pigmentation, prevent, ameliorate or treat immunopathy or immunodeficiency, or regulate body wt. by controlling appetite. These inhibitors are usable in cosmetics and skin preps. for external use. Moreover, they can be easily produced and have a high storage stability.

IT **303728-46-3P 303728-47-4P 303728-48-5P**
303728-49-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(di- and **tripeptid**e derivs. as MSH inhibitors)

RN 303728-46-3 CAPLUS
CN L-Leucinamide, 3-(1-naphthalenyl)-D-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

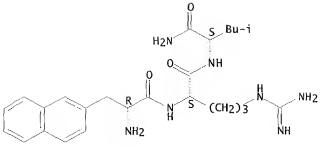
Absolute stereochemistry.

cpds shown in appl. work are novel



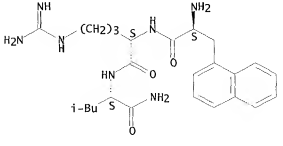
RN 303728-47-4 CAPLUS
CN L-Leucinamide, 3-(2-naphthalenyl)-D-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



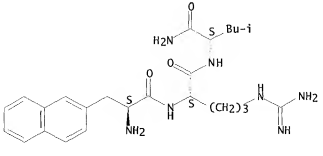
RN 303728-48-5 CAPLUS
CN L-Leucinamide, 3-(1-naphthalenyl)-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 303728-49-6 CAPLUS
CN L-Leucinamide, 3-(2-naphthalenyl)-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:439425 CAPLUS
DOCUMENT NUMBER: 133:204542
TITLE: **Dipeptide** formation on engineered hybrid peptide synthetases
AUTHOR(S): Doekel, Sascha; Marahiel, Mohamed A.
CORPORATE SOURCE: Philipps-Universitat, Fachbereich Chemie/Biochemie, Marburg, 35032, Germany
SOURCE: Chemistry & Biology (2000), 7(6), 373-384
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English

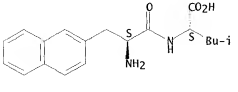
AB Background: Nonribosomal peptide synthetases (NRPSs) are modular megaenzymes that catalyze the assembly of a large no. of bioactive peptides using the multiple carrier thiotemplate mechanism. The modules comprise specific domains that act as distinct units to catalyze specific reactions assocd. with substrate activation, modification and condensation. Such an arrangement of biosynthetic templates has evoked interest in engineering novel NRPSs. Results: We describe the design and construction of a set of dimodular hybrid NRPSs. By introducing domain fusions between adenylation and thiolation (PCP) domains we designed synthetic templates for dipeptide formation. The predicted dipeptides, as defined by the specificity and arrangement of the adenylation domains of the constructed templates, were synthesized in vitro. The effect of the intramol. fusion was investigated by detg. kinetic parameters for substrate adenylation and thiolation. The rate of dipeptide formation on the artificial NRPSs is similar to that of natural templates. Conclusions: Several new aspects concerning the tolerance of NRPSs to domain swaps can be deduced. By choosing the fusion site in the border region of adenylation and PCP domains we showed that the PCP domain exhibits no general substrate selectivity. There was no suggestion that selectivity of the condensation reaction was biased toward the donor amino acid, whereas at the acceptor position there was a size-detd. selection. In addn., we demonstrated that a native elongation module can be converted to an initiation module for peptide-bond formation. These results represent the first example of rational de novo synthesis of small peptides on engineered NRPSs.

IT **290298-01-0P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(**dipeptide** formation on engineered hybrid nonribosomal peptide synthetases)

RN 290298-01-0 CAPLUS

CN L-Leucine, 3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:84636 CAPLUS
DOCUMENT NUMBER: 132:141955
TITLE: Encapsulation of water soluble peptides
INVENTOR(S): Ignatious, Francis X.
PATENT ASSIGNEE(S): Biomeasure Incorporated, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004916	A1	20000203	WO 1999-US14869	19990709 <--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2338345	AA	20000203	CA 1999-2338345	19990709	<--
AU 9949646	A1	20000214	AU 1999-49646	19990709	<--
EP 1098660	A1	20010516	EP 1999-933630	19990709	
EP 1098660	B1	20021016			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002521343	T2	20020716	JP 2000-560909	19990709	
EP 1240896	A2	20020918	EP 2002-76666	19990709	
EP 1240896	A3	20030326			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
AT 226083	E	20021115	AT 1999-933630	19990709	
ES 2185373	T3	20030416	ES 1999-933630	19990709	
US 6270700	B1	20010807	US 1999-357453	19990720	
NO 2001000358	A	20010322	NO 2001-358	20010122	

PRIORITY APPLN. INFO.:

US 1998-121653	A1	19980723
US 1998-93914P	P	19980723
EP 1999-933630	A3	19990709
WO 1999-US14869	W	19990709

AB This invention relates to a process for prepg. biodegradable microspheres and/or nanospheres using an oil-in-water process for the controlled release of bioactive peptides. Thus, of poly(dl-lactide-co-glycolide) (70:30) was mixed with 2% malic acid. NaHCO3 (1N) was added to the polymer and mixed with an aq. soln. of the acetate salt of pyroGlu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH2. Soln. The soln. was stirred for about 2 h and pptd. in 400 mL cold water kept at about 4-6.degree.. The above vacuum dried complex was dissolved in CH2Cl2 (DCM) and the soln. was mixed with 1% PVA soln. The DCM was evapd. off, and the microspheres were collected by centrifugation, suspended in water and lyophilized.

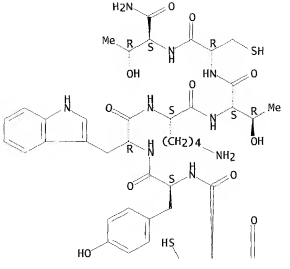
IT **150996-95-5**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(encapsulation of water sol. peptides)

RN 150996-95-5 CAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)

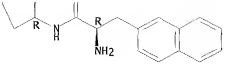
Absolute stereochemistry.

PAGE 1-A



too long

PAGE 2-A



L91 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:325961 CAPLUS
DOCUMENT NUMBER: 130:352553
TITLE: Synthesis of **dipeptide** nitriles as inhibitors of cysteine cathepsins
INVENTOR(S): Altmann, Eva; Betschart, Claudia; Gohda, Keigo; Horiuchi, Miyuki; Lattmann, Rene; Missbach, Martin; Sakaki, Junichi; Takai, Michihiro; Teno, Naoki; Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft mbH
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924460	A2	19990520	WO 1998-EP6937	19981103 <--
WO 9924460	A3	19990902		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2306313	AA	19990520	CA 1998-2306313	19981103	<--
AU 9914873	A1	19990531	AU 1999-14873	19981103	<--
AU 751669	B2	20020822			
EP 1028942	A2	20000823	EP 1998-958887	19981103	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
BR 9813197	A	20000829	BR 1998-13197	19981103	<--
JP 2001522862	T2	20011120	JP 2000-520468	19981103	
RU 2201420	C2	20030327	RU 2000-114821	19981103	
ZA 9810073	A	19990505	ZA 1998-10073	19981104	<--
NO 2000002320	A	20000704	NO 2000-2320	20000502	<--
US 6353017	B1	20020305	US 2000-643639	20000822	

PRIORITY APPLN. INFO.:

GB 1997-23407	A	19971105
US 1997-108160P	P	19971205
US 1997-985973	A	19971205
WO 1998-EP6937	W	19981103
US 1998-186223	B1	19981104

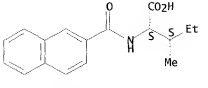
OTHER SOURCE(S): MARPAT 130:352553

AB N-terminal substituted dipeptide nitriles R(L)xX1NHCR2R3C(:Y)NHCR4R5CN [R is optionally substituted aryl, alkyl, alkenyl, alkynyl, heterocyclyl; R2, R3 = H, optionally substituted alkyl, cycloalkyl, bicycloalkyl, or aryl-, biaryl-, cycloalkyl, bicycloalkylalkyl]; R2 and R3 together represent alkylene, optionally interrupted by O, S, or NR6, where R6 is H, alkyl, arylalkyl; or R2 or R3 are linked by alkylene to the adjacent nitrogen to form a ring; R4, R5 = H, optionally substituted alkyl, arylalkyl, CO2R7, CONR7R8 (R7 is optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, or heterocyclyl and R8 is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, heterocyclyl), etc.; R4 and R5 together represent alkylene, optionally interrupted by O, S, or NR6; X1 = CO, CS, SO, SO2, P(O)OR6; Y = O, S: L is optionally substituted Het, Het-CH2, CH2-Het (Het = O, N, or S); x = zero or 1] were prepd. as inhibitors of cysteine cathepsins, e.g., cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions. Thus, N-[2-[(3-carboxyphenyl)methoxy]-1(S)-cyanoethyl]-3-methyl-N.alpha.-(2,2-diphenylacetyl)-L-phenylalaninamide was prepd. and shown to have IC50 .apprxeq. 5 nM for inhibition of cathepsin B.

IT **215096-76-7P 215301-34-1P 225122-28-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of **dipeptide** nitriles as inhibitors of cysteine cathepsins)

RN 215096-76-7 CAPLUS
CN L-Isoleucine, N-(2-naphthalenylcarbonyl)- (9CI) (CA INDEX NAME)

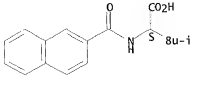
Absolute stereochemistry.



OK

RN 215301-34-1 CAPLUS
CN L-Leucine, N-(2-naphthalenylcarbonyl)- (9CI) (CA INDEX NAME)

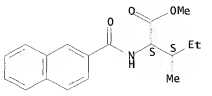
Absolute stereochemistry.



OK

RN 225122-28-1 CAPLUS
CN L-Isoleucine, N-(2-naphthalenylcarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



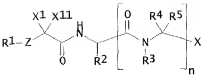
ok

L91 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:352863 CAPLUS
DOCUMENT NUMBER: 129:41414
TITLE: Preparation of N-(phenylacetyl)di- and **tripeptide** derivatives for inhibiting .beta.-amyloid peptide release
INVENTOR(S): Audia, James E.; Britton, Thomas C.; Droste, James J.; Folmer, Beverly K.; Huffman, George W.; John, Varghese; Latimer, Lee H.; Mabry, Thomas E.; Nissen, Jeffrey S.; et al.
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; Eli Lilly & Co.; Audia, James E.; Britton, Thomas C.; Droste, James J.; Folmer, Beverly K.; Huffman, George W.; John, Varghese
SOURCE: PCT Int. Appl., 487 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822494	A2	19980528	WO 1997-US20804	19971121 <--
WO 9822494	A3	19981126		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9710470	A	19980625	ZA 1997-10470	19971120 <--
AU 9853561	A1	19980610	AU 1998-53561	19971121 <--
EP 942924	A2	19990922	EP 1997-950601	19971121 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1238779	A	19991215	CN 1997-199803	19971121 <--
BR 9713400	A	20000125	BR 1997-13400	19971121 <--
JP 2001503782	T2	20010321	JP 1998-523756	19971121
NO 9902368	A	19990621	NO 1999-2368	19990514 <--
MX 9904744	A	20000731	MX 1999-4744	19990521 <--

PRIORITY APPLN. INFO.:	US 1996-755442	A	19961122
	US 1997-807427	A	19970228
	US 1997-807528	A	19970228
	US 1997-808528	A	19970228
	WO 1997-US20804	W	19971121

OTHER SOURCE(S): MARPAT 129:41414
GI



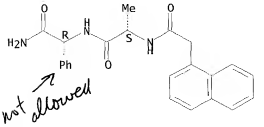
I

AB Disclosed are compds. I [R1 = aryl, heteroaryl, heterocyclyl, optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, or cycloalkenyl; R2 = H, any group R1; each R3 = H, Me; R3-R4 may form optionally fused cyclic structure of 3-8 atoms; each R4 = any group R2; each R5 = H, Me; R4-R5 may form a C3-6 cycloalkyl group; X = CO-Y, CS-Y; Y = OH, aryl, heteroaryl, heterocyclyl, optionally substituted alkyl, cycloalkyl, alkoxy, thioalkoxy, amino, etc.; X1 = H, OH, F; X11 = H, OH, F; or X1X11 = O; Z = bond, O, S; n = 1, 2] and pharmaceutically acceptable salts thereof, which inhibit .beta.-amyloid peptide release and/or its synthesis, and, accordingly, have utility in treating Alzheimer's disease. Also disclosed pharmaceutical compns. comprising a compd. which inhibits .beta.-amyloid peptide release and/or its synthesis as well as methods for treating Alzheimer's disease both prophylactically and therapeutically with such pharmaceutical compns. Over 400 title compds., e.g. 3,5-F2C6H3CH2CO-L-Ala-L-Nle-OMe, were prepd. and screened for inhibition of .beta.-amyloid prodn. Formulations for pharmaceutical compns. are also given.

IT **208258-51-9P 208258-52-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(phenylacetyl)di- and **tripeptide** derivs. for inhibiting .beta.-amyloid peptide release)

RN 208258-51-9 CAPLUS
CN Glycinamide, N-(1-naphthalenylacetyl)-L-alanyl-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

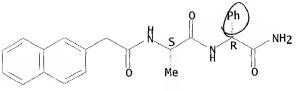
Absolute stereochemistry.



not allowed

RN 208258-52-0 CAPLUS
CN Glycinamide, N-(2-naphthalenylacetyl)-L-alanyl-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

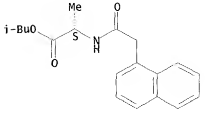
Absolute stereochemistry.



IT **208116-35-2P 208116-36-3P 208116-49-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-(phenylacetyl)di- and **tripeptide** derivs. for

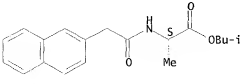
inhibiting .beta.-amyloid peptide release)
RN 208116-35-2 CAPLUS
CN L-Alanine, N-(1-naphthalenylacetyl)-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



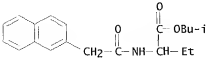
RN 208116-36-3 CAPLUS
CN L-Alanine, N-(2-naphthalenylacetyl)-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



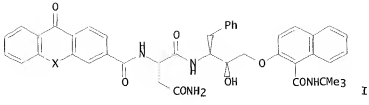
ok

RN 208116-49-8 CAPLUS
CN Butanoic acid, 2-[(2-naphthalenylacetyl)amino]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



ok

L91 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:310423 CAPLUS
DOCUMENT NUMBER: 129:54583
TITLE: Novel HIV- protease inhibitors containing .beta.-hydroxyether and -thioether **dipeptide** isostere surrogates: modification of the P3 ligand
AUTHOR(S): Patel, Naginbhai M.; Bennett, Frank; Girijavallabhan, Viyyoor M.; Dasmahapatra, Bimalendu; Butkiewicz, Nancy; Hart, Andrea
CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(8), 931-934
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

bad

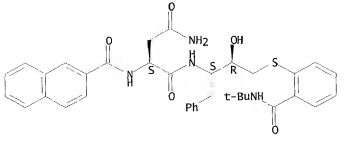
AB Studies involving modifications to the P3 position of previously described HIV-protease inhibitors contg. .beta.-hydroxyether and thioether dipeptide isostere replacements led to the discovery of pseudopeptides I (X = CO, SO2) with improved antiviral activities.

IT **149451-35-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of novel HIV protease inhibitors contg. hydroxyether and thioether **dipeptide** isostere surrogates)

RN 149451-35-4 CAPLUS

CN Butanediamide, N1-[(1S,2R)-3-[[2-[[[(1,1-dimethylethyl)amino]carbonyl]phenyl]thio]-2-hydroxy-1-(phenylmethyl)propyl]-2-[(2-naphthalenylcarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



bad

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:220603 CAPLUS
DOCUMENT NUMBER: 126:212446
TITLE: **Tripeptide** methyl ketone cysteine protease inhibitors for use in treatment of Ige mediated allergic diseases
INVENTOR(S): Johnson, Tony; Hart, Terrance; Laing, Peter; Shakib, Farouk; Quibell, Martin
PATENT ASSIGNEE(S): Peptide Therapeutics Limited, UK; Johnson, Tony; Hart, Terrance; Laing, Peter; Shakib, Farouk; Quibell, Martin
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704004	A1	19970206	WO 1996-GB1707	19960717 <--

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,

EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM

AU 9665242	A1	19970218	AU 1996-65242	19960717	<--
AU 716716	B2	20000302			
EP 839155	A1	19980506	EP 1996-924976	19960717	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11509543	T2	19990824	JP 1996-506421	19960717	<--
US 6034066	A	20000307	US 1998-45	19980226	<--
PRIORITY APPLN. INFO.:			GB 1995-14616	19950717	
			GB 1995-22221	19951031	
			WO 1996-GB1707	19960717	

OTHER SOURCE(S): MARPAT 126:212446

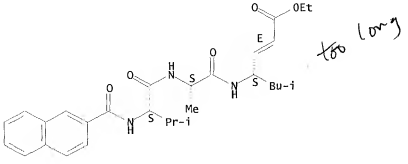
AB Tripeptide compds. were prepd for use in the treatment of allergic diseases, including juvenile asthma and eczema, via inhibition of the cysteine protease activity of Dermatophagoides pteronyssinus (Der p I), a major allergen of house dust mite. Compds. claimed included R1-CONH-XR2-CONH-YR3-CONH-ZR4-W [X, Y, Z = N, CH; R1 = nitrogen blocking group; R2, R3, R4 = side-chains on X, Y, Z; W = group that reacts irreversibly with active cysteine thiol of Der p I; R1 = hydrophobic Ph, 2-naphthyl, 9-anthracyl, heteroaryl optionally connected to heteroatom to carbonyl group, etc.; XR2 = Ala, Leu, Nle, Val, etc; YR3 = Lys, Gln, Met(O), Ala; ZR4 = Ala, Leu, Nle, Val, Ile, etc.; W = E-CH2CHO, E-CH2CH:CH2, E-CH2CH:CHCHO, R-CO2NCHO, Y-CH:CH2; E = aryloxy, arylthio, heteroaryl, halo, R-SO3, R2P(O)O, RCO2; R = alkyl, aryl; Y = ester, sulfone, carboxylate, amide, etc. groups]. E64, L-trans-epoxysuccinyl-leucylamido(4-guanidino)butane, is excluded from the claimed compds. Thus, Bz-Val-Ala-Nle-OH underwent successive treatment with iso-Bu chloroformate/N-methylmorpholine, CH2N2, and HBr/HOAc to give Bz-Val-Ala-Nle-CH2Br which reacted with 2,6-Cl2C6H3CO2OH to give Bz-Val-Ala-Nle-CH2O2CC6H3Cl2-2,6 (I). In Der p I enzyme inhibiting assay, I had a Kobs/[I] of 6.8 x 107 M-1 s-1.

IT **187991-69-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of **tripeptide** Me ketones with allergen inhibiting activity)

RN 187991-69-1 CAPLUS

CN L-Alaninamide, N-(2-naphthalenylcarbonyl)-L-valyl-N-[(1S,2E)-4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L91 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1996:593835 CAPLUS
DOCUMENT NUMBER:	125:248489
TITLE:	Preparation of **dipeptide** derivatives as cell adhesion inhibitors
INVENTOR(S):	Adams, Steven P.; Lin, Ko-Chung; Lee, Wen-Cherng;

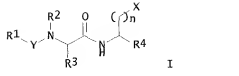
Castro, Alfredo C.; Zimmerman, Craig N.; Hammond, Charles E.; Liao, Yu-Sheng; Cuervo, Julio Hernan; Singh, Juswinder

PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

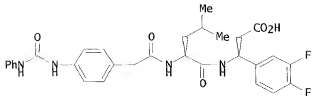
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9622966	A1	19960801	WO 1996-US1349	19960118	<--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE					
US 6306840	B1	20011023	US 1995-376372	19950123	
CA 2211181	AA	19960801	CA 1996-2211181	19960118	<--
AU 9649115	A1	19960814	AU 1996-49115	19960118	<--
AU 718926	B2	20000504			
EP 805796	A1	19971112	EP 1996-905316	19960118	<--
EP 805796	B1	20021211			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI					
BR 9606778	A	19980106	BR 1996-6778	19960118	<--
CN 1177343	A	19980325	CN 1996-192270	19960118	<--
JP 10513160	T2	19981215	JP 1996-523071	19960118	<--
EP 1142867	A2	20011010	EP 2001-107877	19960118	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI					
AT 229498	E	20021215	AT 1996-905316	19960118	
ES 2183937	T3	20030401	ES 1996-905316	19960118	
CZ 291556	B6	20030416	CZ 1997-2340	19960118	
TW 500714	B	20020901	TW 1996-85100690	19960122	
NO 9703384	A	19970919	NO 1997-3384	19970722	<--
FI 9703087	A	19970922	FI 1997-3087	19970722	<--
BG 63383	B1	20011231	BG 1997-101841	19970821	
US 6376538	B1	20020423	US 1997-875321	19970919	
US 2003083267	A1	20030501	US 2001-935461	20010822	
US 2003018016	A1	20030123	US 2001-2341	20011023	

PRIORITY APPLN. INFO.:
US 1995-376372 A2 19950123
EP 1996-905316 A3 19960118
WO 1996-US1349 W 19960118
US 1997-875321 A3 19970919

OTHER SOURCE(S): MARPAT 125:248489
GI



I



II

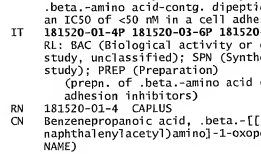
AB Novel dipeptide analogs I [X = CO2H, PO3H-, SO2R5, SO3H, OPO3H-, CO2R4, CONR42; Y = CO, SO2, PO2; n = 0-2; R1 = optionally substituted alkyl, alkenyl, alkynyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl, alkoxy, alkenyloxy, aralkoxy, alkylamino, alkenylamino, alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, heterocyclyl; R2 = H, aryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl-substituted alkyl; R2NCR3 = heterocyclic ring; R3 = natural, unnatural, modified, or substituted amino acid side chain; R4 = optionally substituted aryl, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl-substituted alkyl, H, heterocyclyl, heterocyclylcarbonyl, aminocarbonyl, amido, alkylaminocarbonyl, arylaminocarbonyl, acylaminocarbonyl, acyl; R5 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl] are prepd. as compds. useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical compns. of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, .beta.-amino acid-contg. dipeptide II, prepd. by std. methods, displayed an IC50 of <50 nM in a cell adhesion inhibition assay.

IT **181520-01-4P 181520-03-6P 181520-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of .beta.-amino acid **dipeptide** derivs. as cell adhesion inhibitors)

RN 181520-01-4 CAPLUS

CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(1-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

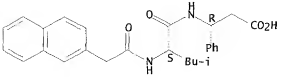
Absolute stereochemistry.



RN 181520-03-6 CAPLUS

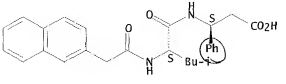
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



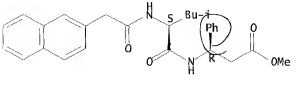
RN 181520-87-6 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



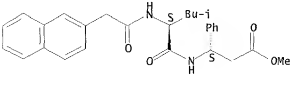
IT **181518-17-2P 181518-19-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .beta.-amino acid **dipeptide** derivs. as cell adhesion inhibitors)
RN 181518-17-2 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 181518-19-4 CAPLUS
CN Benzenepropanoic acid, .beta.-[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



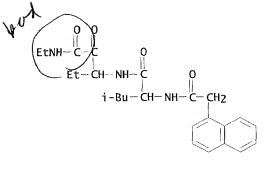
=> d ibib abs hitstr 11-25

L91 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:544115 CAPLUS
DOCUMENT NUMBER: 125:237576
TITLE: Novel Peptidyl .alpha.-Keto Amide Inhibitors of Calpains and Other Cysteine Proteases
AUTHOR(S): Li, Zhaozhao; Ortega-Vilain, Anne-Cecile; Patil, Girish S.; Chu, Der-Lun; Foreman, J. E.; Eveleth, David D.; Powers, James C.
CORPORATE SOURCE: School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332-0400, USA
SOURCE: Journal of Medicinal Chemistry (**1996**), 39(20), 4089-4098
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of new dipeptidyl .alpha.-keto amides of the general structure R1-L-Leu-D,L-AA-CONH-R2 were synthesized and evaluated as inhibitors for the cysteine proteases calpain I, calpain II, and cathepsin B. They combine 10 different N-protecting groups (R1), 3 amino acids residues in P1 (AA), and 44 distinct substituents on the .alpha.-keto amide nitrogen (R2). In general, calpain II was more sensitive to these inhibitors than calpain I, with a large no. of inhibitors displaying dissocn. consts. (Ki) in the 10-100 nM range. Calpain I was also effectively inhibited, but very low Ki values were obsd. with a smaller no. of inhibitors than with calpain II. Cathepsin B was weakly inhibited by most compds. in this study. The best inhibitors for calpain II were Z-Leu-Abu-CONH-CH2-CHOH-C6H5 (Ki = 15 nM), Z-Leu-Abu-CONH-CH2-2-pyridyl (Ki = 17 nM), and Z-Leu-Abu-CONH-CH2-C6H3(3,5(OMe)2) (Ki = 22 nM). The best calpain I inhibitor in this study was Z-Leu-Nva-CONH-CH2-2-pyridyl (Ki = 19 nM). The peptide .alpha.-keto amide Z-Leu-Abu-CONH-(CH2)2-3-indolyl was the best inhibitor for cathepsin B (Ki = 31 nM). Some compds. acted as specific calpain inhibitors, with comparable activity on both calpains I and II and a lack of activity on cathepsin B. Others were specific inhibitors for calpain I (e.g., 73) or calpain II. Such inhibitors may be useful in elucidating the physiol. and pathol. events involving these proteases and may become possible therapeutic agents.

IT **178675-63-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of novel peptidyl .alpha.-keto amide inhibitors of calpains and other cysteine proteases)

RN 178675-63-3 CAPLUS
CN 1-Naphthaleneacetamide, N-[1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

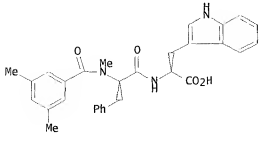


L91 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:887871 CAPLUS
DOCUMENT NUMBER: 123:340965
TITLE: Preparation of **dipeptide** analogs as endothelin receptor antagonists.

INVENTOR(S): Saika, Hideyuki; Murata, Toshiki; Pitterna, Thomas; Frueh, Thomas; Svensson, Lene D.; Urade, Yoshihiro; Yamamura, Takaki; Okada, Toshikazu
PATENT ASSIGNEE(S): Japat Ltd., Switz.; Ciba-Geigy Japan Ltd.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9512611	A1	19950511	WO 1994-EP3418	19941017 <--
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2173875	AA	19950511	CA 1994-2173875	19941017 <--
AU 9478565	A1	19950523	AU 1994-78565	19941017 <--
AU 691201	B2	19980514		
EP 728145	A1	19960828	EP 1994-929557	19941017 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9407933	A	19961126	BR 1994-7933	19941017 <--
JP 09504302	T2	19970428	JP 1994-512982	19941017 <--
RU 2126418	C1	19990220	RU 1996-112148	19941017 <--
ZA 9408541	A	19950502	ZA 1994-8541	19941031 <--
FI 9601804	A	19960430	FI 1996-1804	19960426 <--
NO 9601725	A	19960429	NO 1996-1725	19960429 <--
US 5780498	A	19980714	US 1996-637720	19960430 <--

PRIORITY APPLN. INFO.: EP 1993-810760 A 19931101
WO 1994-EP3418 W 19941017
OTHER SOURCE(S): MARPAT 123:340965
GI



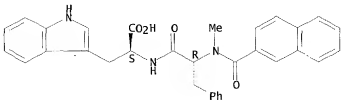
I

AB R1CONR2CH(CR3R31R311)C(X)YCHR4R5 [R1 = alkyl, cycloalkylalkyl, aralkyl, cycloalkyl, aryl, arylcycloalkyl, alkoxy, aryloxy, heteroaryl; R2 = H, alkyl, cycloalkyl, cycloalkylalkyl; R3, R31 = H, alkyl, cycloalkyl, aralkyl, aryl, heteroaryl; R3R31 = atoms to form a ring; R311 = H, alkyl, aryl; R2R311 = (CH2)n, (CH2)pAr; n = 1, 2, 3; p = 0, 1, 2; Ar = (hetero)arylene; X = O, S, NH, NHOH, CH2, etc.; Y = bond, O, CH2, imino; or X = (H, OH) and Y = bond, CH2; R4 = (CH2)sAr1; s = 0, 1, 2, 3; Ar1 = (hetero)aryl; R5 = H, carboxy, (substituted) carboxamido, PO(OH)2, tetrazolyl, CH2OH, CN], were prepd. Thus, title compd. (I), prepd. by soln. phase means, inhibited endothelin-3 induced contraction of guinea pig trachea with pA2 = 6.3. Drug formulations contg. I are given.

IT **169544-93-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

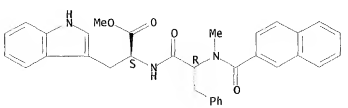
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **dipeptide** analogs as endothelin receptor antagonists)
RN 169544-93-8 CAPLUS
CN L-Tryptophan, N-[N-methyl-N-(2-naphthalenylcarbonyl)-D-phenylalanyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **169546-10-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **dipeptide** analogs as endothelin receptor antagonists)
RN 169546-10-5 CAPLUS
CN L-Tryptophan, N-[N-methyl-N-(2-naphthalenylcarbonyl)-D-phenylalanyl]-, methyl ester (9CI) (CA INDEX NAME)

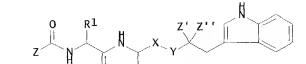
Absolute stereochemistry.



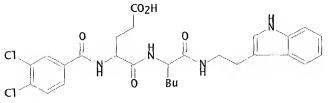
L91 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:758608 CAPLUS
DOCUMENT NUMBER: 123:170184
TITLE: New pseudo-**dipeptide** derivatives, their preparation, and their use as gastrin antagonists.
INVENTOR(S): Martinez, Jean; Riquet, William; Bigg, Dennis; Halazy, Serge
PATENT ASSIGNEE(S): Fabre Pierre Medicament, Fr.
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2697843	A1	19940513	FR 1992-13542	19921110 <--
WO 9411390	A1	19940526	WO 1993-FR1099	19931109 <--

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: FR 1992-13542 19921110
OTHER SOURCE(S): MARPAT 123:170184
GI



I



II

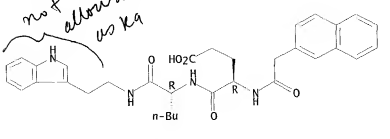
AB Title compds. I [Z = (un)substituted Ph, PhCH2, indanyl, (poly)cycloalkyl, indolylalkyl, naphthyl, naphthylmethyl, PhOCH2, naphthoxymethyl; R1 = (CH2)nCO2H; n = 1-5; R2 = alkyl; X = NH or CO; Y = CO or NH; X .noteq. Y; Z' = H, Me; Z'' = H, CO2R3, NHCO2R3; if Y = NH, Z'' .noteq. NHCOR3; if Y = CO, Z'' .noteq. COR3; R3 = (un)substituted alkyl, (poly)cycloalkyl, Ph] and salts are claimed and prepd. (14 examples). I are gastrin and CCK receptor antagonists, and are claimed useful for treating ulcers, Zollinger-Ellison syndrome, and reflux-induced esophagitis. For example, amidation of tryptamine with Boc-D-Nle-OSu [Boc = tert-BuOCO, Su = N-succinimidyl] in DMF gave 79% Boc-D-Nle-NHCH2CH2R [R = 3-indolyl]. This was deprotected with CF3CO2H and coupled with Z-D-Glu(OCH2Ph)-ONp [Z = PhCH2OCO, Np = C6H4NO2-p] in DMF in the presence of HOBT and DIEA to give 94% Z-D-Glu(OCH2Ph)-D-Nle-NHCH2CH2R. Hydrogenolysis of the latter compd. and coupling with 3,4-Cl2C6H3CO2Su in DMF in the presence of DIEA gave title compd. D,D-II. In the EtOH-induced ulcer test in mice, this compd. gave 80% inhibition at 25 mg/kg p.o.

IT **166945-25-1P 166945-26-2P 166945-27-3P**
166945-28-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pseudo-**dipeptides** as gastrin and CCK antagonists)

RN 166945-25-1 CAPLUS

CN D-Norleucinamide, N-(2-naphthalenylacetyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

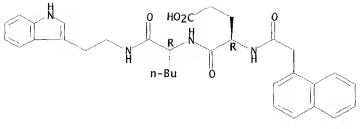
Absolute stereochemistry.



RN 166945-26-2 CAPLUS

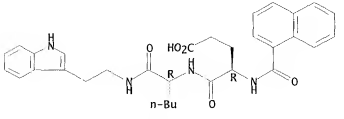
CN D-Norleucinamide, N-(1-naphthalenylacetyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



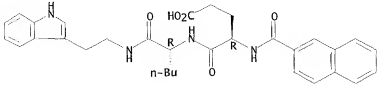
RN 166945-27-3 CAPLUS
CN D-Norleucinamide, N-(1-naphthalenylcarbonyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 166945-28-4 CAPLUS
CN D-Norleucinamide, N-(2-naphthalenylcarbonyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

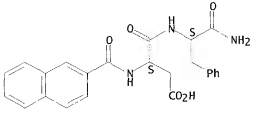
Absolute stereochemistry.



L91 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:245758 CAPLUS
DOCUMENT NUMBER: 120:245758
TITLE: 2-NAP: a selective, hydrophilic, non-peptide CCKA - receptor antagonist derived from the cholecystokinin C-terminal **dipeptide**
AUTHOR(S): McDonald, Iain M.; Bodkin, Michael J.; Broughton, Howard B.; Dunstone, David J.; Kalindjian, S. Barret; Low, Caroline M. R.
CORPORATE SOURCE: Sch. Med. Dent., King's Coll., London, SE24 9JE, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (**1993**), 3(8), 1511-16
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of the cholecystokinin (CCK) C-terminal dipeptide(32-33) (H-Asp-Phe-NH2) have been prepd. and the structure-activity relationships of this series are described. The sodium salt of 2-naphthalenesulfonyl-L-aspartyl (2-phenethyl)amide, (2-NAP), displayed high affinity for CCKA receptors by its antagonism of CCK8-stimulated guinea-pig gallbladder contraction. In addn., 2-NAP exhibits selectivity with respect to

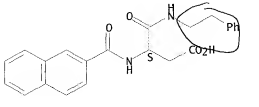
gastrin/CCK8 receptors (>300-fold) and has a low log P (-0.91, chloroform/buffer).
IT **154510-45-9 154510-51-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cholecystokinin A receptor antagonist activity of)
RN 154510-45-9 CAPLUS
CN L-Phenylalaninamide, N-(2-naphthalenylcarbonyl)-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154510-51-7 CAPLUS
CN Butanoic acid, 3-[(2-naphthalenylcarbonyl)amino]-4-oxo-4-[(2-phenylethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

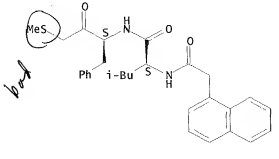


L91 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:496186 CAPLUS
DOCUMENT NUMBER: 119:96186
TITLE: Preparation of pseudopeptides and **dipeptides** characterized by a substituted methyl ketone moiety at the C-terminus as thiol protease inhibitors
INVENTOR(S): Ando, Ryoichi; Ando, Naoko; Masuda, Hirokazu; Morinaka, Yasuhiro; Takahashi, Chizuko; Tamao, Yoshikuni; Tobe, Akihiro
PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan
SOURCE: Eur. Pat. Appl., 218 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 525420	A1	19930203	EP 1992-111129	19920701 <--
EP 525420	B1	19990512		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
JP 05246968	A2	19930924	JP 1992-165094	19920623 <--
JP 3190431	B2	20010723		
CA 2072834	AA	19930102	CA 1992-2072834	19920630 <--
AT 179974	E	19990515	AT 1992-111129	19920701 <--
ES 2132096	T3	19990816	ES 1992-111129	19920701 <--
US 5639783	A	19970617	US 1995-451720	19950526 <--

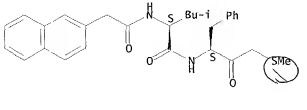
US 5834508 A 19981110 US 1997-798036 19970206 <--
PRIORITY APPLN. INFO.: JP 1991-160674 A 19910701
JP 1991-277905 A 19911024
JP 1991-343668 A 19911225
US 1992-907228 B1 19920701
US 1994-252397 B1 19940601
US 1995-451720 A3 19950526
OTHER SOURCE(S): MARPAT 119:96186
AB R1(NR2CHR3CO)nNR4CHR5CONR6CR7R8COCH2AR9 [R1 = H, R10CO, R10O2C, R10SO2, R10NHCO; R2; R4, R6 = H, alkyl; R3, R5 = alkoxy, H, aralkoxy, (substituted) aryl, alkyl; R2R3, R4R5 = (substituted) heterocyclyl; R7 = H, (substituted) alkyl, aralkoxy, aryl, alkoxy; R8 = H, alkyl, (substituted) aralkyl; R7R8 = (substituted) benzylidene, cycloalkyl; A = S, SO, SO2, O, NH, alkylimino; R9 = H, (substituted) aryl, (CH2)nX; n = 0, 1; m = 0-15; X = H, OH, alkylthio, alkoxycarbonylamino, (substituted) heterocyclyl, amino, arylamino, halo, alkoxy, (substituted) aryl, aryloxy; R10 = (substituted) alkyl], were prepd. Thus, S-3-amino-1-furfurylthio-2-heptanone hydrochloride (prepn. given) was condensed with tert-butoxycarbonylleucine N-hydroxysuccinimido ester in CH2Cl2 contg. Et3N to give 96% S-3-(S-2-tert-butoxycarbonylamino-4-methylvalerylamino)-1-furfurylthio-2-heptanone. This inhibited papain, cathepsin B, cathepsin L, and m-calpain with IC50's of 0.37, 0.057, 0.038, and 5.8 .mu.m, resp. Dosage forms were prepd. contg. specific title compds.
IT **149044-24-6P 149044-25-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as thiol protease inhibitor)
RN 149044-24-6 CAPLUS
CN 1-Naphthaleneacetamide, N-[3-methyl-1-[[[3-(methylthio)-2-oxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 149044-25-7 CAPLUS
CN 2-Naphthaleneacetamide, N-[3-methyl-1-[[[3-(methylthio)-2-oxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

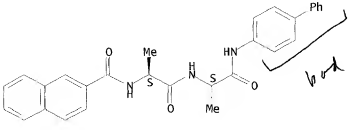
Absolute stereochemistry.



L91 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:7376 CAPLUS
DOCUMENT NUMBER: 118:7376
TITLE: Peptide conformational analysis using the TRIPOS force

field
AUTHOR(S): Wall, Craig G.; Healy, Eamonn F.; Fox, Marye Anne
CORPORATE SOURCE: Dep. Chem., Univ. Texas, Austin, TX, 78712, USA
SOURCE: International Journal of Quantum Chemistry (1992), 44(4), 543-8
CODEN: IJQCB2; ISSN: 0020-7608
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A conformational anal. of the dipeptide 2-C10H7CO-Ala-Ala-NHC6H4Ph-4 (I) was performed using a std. mol. mechanics force field. to explain obsd. electron transfer rates between the terminal arom. moieties. The resulting low-energy conformers could conveniently be grouped into two families with an av. energy difference of ca. 2 kcal mol-1 and populations of 64% and 30%, resp. These results correlate well with the 78:22 ratio of the two exptl. distinguishable decay processes for the radical anion of I.
IT 135311-05-6
RL: PROC (Process)
(conformational anal. of, by mol. mechanics)
RN 135311-05-6 CAPLUS
CN L-Alaninamide, N-(2-naphthalenylcarbonyl)-L-alanyl-N-[1,1'-biphenyl]-4-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:806 CAPLUS
DOCUMENT NUMBER: 118:806
TITLE: Method of treating benign and malignant proliferative skin disease by topical administration of a somatostatin analog
INVENTOR(S): Bogden, Arthur E.; Moreau, Jacques Pierre
PATENT ASSIGNEE(S): Biomeasure, Inc., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9213554	A1	19920820	WO 1992-US1027	19920207	<--
W: CA, CS, FI, HU, JP, NO, RU					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
EP 542934	A1	19930526	EP 1992-906420	19920207	<--
EP 542934	B1	19990616			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
JP 05506254	T2	19930916	JP 1992-505872	19920207	<--
AT 181240	E	19990715	AT 1992-906420	19920207	<--
ES 2134798	T3	19991016	ES 1992-906420	19920207	<--
US 6087337	A	20000711	US 1993-89410	19930709	<--
PRIORITY APPLN. INFO.:			US 1991-652863 A	19910208	
			WO 1992-US1027 W	19920207	

OTHER SOURCE(S): MARPAT 118:806

AB A compn. for treating a mammal suffering from benign or malignant proliferative skin disease comprises an effective amt. of a somatostatin analog contg. .gtoreq.6 amino acids, formulated with an excipient suitable for topical administration to the mammal. D-.beta.-Naphthyl-Ala-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2 was synthesized on benzhydrylamine-polystyrene resin. B16-F10 **melanoma** xenografts in mice were treated with topical somatuline.

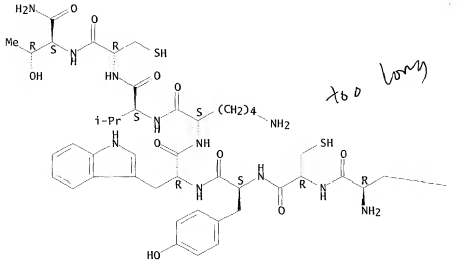
IT **113294-82-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of benign or malignant proliferative skin disease)

RN 113294-82-9 CAPLUS

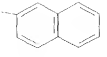
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

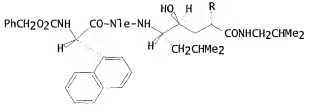
PAGE 1-A



PAGE 1-B



L91 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:470294 CAPLUS
DOCUMENT NUMBER: 117:70294
TITLE: Renin inhibitors. I. Synthesis and structure-activity relationships of transition-state inhibitors containing homostatine analogs at the scissile bond
AUTHOR(S): Atsuumi, Shugo; Nakano, Masato; Koike, Yutaka; Tanaka, Seiichi; Matsuyama, Kenji; Nakano, Makiko; Morishima, Hajime
CORPORATE SOURCE: Explor. Res. Lab., Banyu Pharm. Co., Ltd., Tokyo, 153, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1992), 40(2), 364-70
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

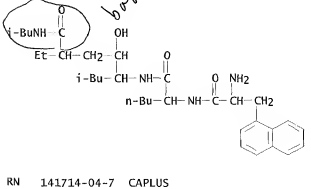


I

AB The synthesis and structure-activity relationships of transition-state renin inhibitors, e.g. I [R = H, Me, Et, Pr, CHMe2, CH2CHMe2, Me3CO2CNHCH2, HOCH2CH2, HOCH2CH2CH2, H2NCH2CH2CH2 HOCHMeCH2, HOCH2CH(OH)CH2), contg. the homostatine analogs at the scissile bond are described. These inhibitors incorporate the amino acid side chains corresponding to positions 7-12 (P4-P2') of angiotensinogen. Et, 2-hydroxyethyl, and 3-hydroxypropyl groups at position 2 of the homostatine analogs (P1') are more effective for increasing potency than the iso-Pr group. A combination of residues at P1, P3, and P4 is important for potency and this result suggests that S1, S3, and S4 form a huge hydrophobic core together in renin.

IT **141713-99-7 141714-04-7 141782-86-7**
141783-51-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(renin inhibitory activity of)

RN 141713-99-7 CAPLUS
CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)



RN 141714-04-7 CAPLUS

CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-4-[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

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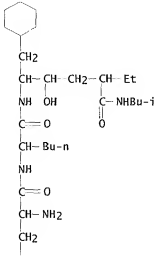

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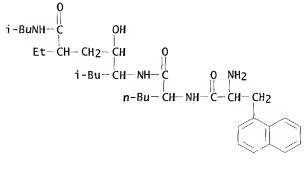
RN 141782-86-7 CAPLUS
CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)



RN 141783-51-9 CAPLUS
CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-4-[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R,4S*)]- (9CI) (CA INDEX NAME)

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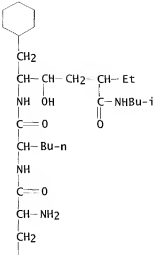

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L91 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:256009 CAPLUS
DOCUMENT NUMBER: 116:256009
TITLE: Development of potent and selective CCK-A receptor agonists from Boc-CCK-4: tetrapeptides containing Lys(N.epsilon.)-amide residues
AUTHOR(S): Shiosaki, Kazumi; Lin, Chun Wei; Kopecka, Hana; Craig, Richard A.; Bianchi, Bruce R.; Miller, Thomas R.; Witte, David G.; Stashko, Michael; Nadzan, Alex M.
CORPORATE SOURCE: Neurosci. Res. Div., Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(11), 2007-14
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of Boc-CCK-4 (Boc = CO2CMe3) derivs. represented by the general structure Boc-Trp-Lys(COR)Asp-Phe-NH2, where R is an arom., heterocyclic, or aliph. group, are potent and selective CCK-A receptor agonists. These amide-bearing compds. complement the previously described urea-based tetrapeptides (Shiosaki et al. 1991); structure activity studies revealed parallel as well as divergent trends between these two series. A significant correlation was obsd. between pancreatic binding affinity and the resonance const. .vphi..SCRIPTR. of the Ph substituent in one particular series of derivs. Sulfation of phenolic amides appended onto the .epsilon.-amino group of the lysine did not affect affinity for the CCK-A receptor in contrast to the 500-fold increase in binding potency obsd. upon sulfation of CCK-8, suggesting that the lysine appendage and the sulfated tyrosine in CCK-8, both key structural elements that impart high affinity for the CCK-A receptor, are interacting differently with the receptor. The amide-bearing tetrapeptides are full agonists relative to

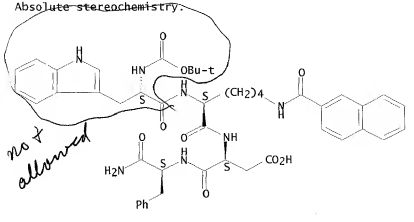
CCK-8 in stimulating pancreatic amylase release while being partial agonists in eliciting phosphoinositide (PI) hydrolysis. Both effects were blocked by selective CCK-A receptor antagonists.

IT 131449-07-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as selective CCK-A receptor agonist)

RN 131449-07-5 CAPLUS

CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-N6-(2-naphthalenylcarbonyl)-L-lysyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:152363 CAPLUS

DOCUMENT NUMBER: 116:152363

TITLE: Conformational preferences of oligopeptides rich in .alpha.-aminoisobutyric acid. I. Observation of a 310/.alpha.-helical transition upon sequence permutation

AUTHOR(S): Basu, Gautam; Bagchi, Ken; Kuki, Atsuo

CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA

SOURCE: Biopolymers (1991), 31(14), 1763-74
CODEN: BIPMAA; ISSN: 0006-3525

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The soln. conformation of peptides rich in .alpha.-aminoisobutyric acid (Aib) is a subtle problem, not because of helix/coil transitions, but rather because of .alpha.-helical/310-helical competition. A series of peptides contg. 75% Aib has been synthesized that feature identical amino acid compn. but differing sequences; they are sequence permutation isomers. NMR hydrogen-bonding studies reveal that there is a sequence permutation-induced transition between the 2 alternative helical forms within this set. The implications for the design and conformational prediction of helical Aib-rich peptides are discussed.

IT 139881-89-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with aminoisobutyric acid **dipeptide** oxazolone)

RN 139881-89-3 CAPLUS

CN Alaninamide, 3-(1-naphthalenyl)-L-alanyl-2-methylalanyl-L-phenylalanyl-2-methylalanyl-2-methylalanyl-N,2-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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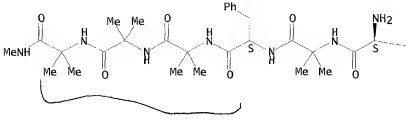

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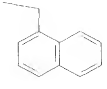
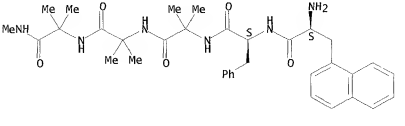


IT **139881-88-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with aminoisobutyric acid **tripeptide**)
RN 139881-88-2 CAPLUS
CN Alaninamide, 3-(1-naphthalenyl)-L-alanyl-L-phenylalanyl-2-methylalanyl-2-methylalanyl-N,2-dimethyl- (9CI) (CA INDEX NAME)

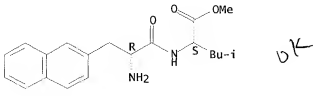
Absolute stereochemistry.



L91 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:498001 CAPLUS
DOCUMENT NUMBER: 113:98001
TITLE: Novel inhibitors of human renin unrelated to the angiotensinogen sequence. Analogs of a tetrapeptide, Boc-D-Phe-Cys(Acm)-D-Trp-Leu-OMe
AUTHOR(S): Dutta, Anand S.; Gormley, James J.; McLachlan, Peter F.; Major, John S.
CORPORATE SOURCE: Chem. Dep., ICI Pharm., Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Journal of Chemical Research, Synopses (**1990**), (1), 2-3
CODEN: JRPSDC; ISSN: 0308-2342
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eighty-three title peptides analogs were prepd. by conventional soln. methods. Renin-inhibiting activation were detd. and structure-activity relationships were discussed.
IT **128730-83-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

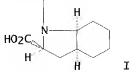
(prepn. and peptide coupling of, with cysteine deriv.)
RN 128730-83-6 CAPLUS
CN L-Leucine, N-[3-(2-naphthalenyl)-D-alanyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:478951 CAPLUS
DOCUMENT NUMBER: 113:78951
TITLE: Angiotensin-converting enzyme inhibitors: synthesis and biological activity of N-substituted **tripeptide** inhibitors
AUTHOR(S): Sawayama, Tadahiro; Tsukamoto, Masatoshi; Sasagawa, Takashi; Nishimura, Kazuya; Deguchi, Takashi; Takeyama, Kunihiko; Hosoki, Kanoo
CORPORATE SOURCE: Res. Lab., Dainippon Pharm. Co., Ltd., Suita, 564, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (**1990**), 38(1), 110-15
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:78951
GI

RCO-Lys-D-Glu-OH



I

AB A new series of highly potent angiotensin-converting enzyme inhibitors, 1-(N2-substituted L-lysyl-.gamma.-D-glutamyl)octahydro-1H-indole-2-carboxylic acids I (R = aryl, aralkyloxy, cycloalkyloxy, amino) was prepd.; various acyl groups were introduced at the .alpha.-amino group of the N-terminal lysine. The effect of the N2-acyl groups on in vitro inhibitory activity and oral antihypertensive effect was examd. All of the synthesized N-acyl tripeptides have in vitro inhibitory activity at an approx. nanomolar level, and showed antihypertensive potency in renal hypertensive rats at a dose of 10 mg/kg, when administered orally. Among them, compds. I (R = 2-ClC6H4CH2O, 2-FC6H4CH2O, 4-FC6H4, 4-HOC6H4, 3-pyridyl) showed potent and long-lasting antihypertensive effects compared with enalapril. Their structure-activity relationships are also discussed.
IT **128595-16-4P 128595-17-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and inhibition by, of angiotensin-converting enzyme)
RN 128595-16-4 CAPLUS
CN D-Norvaline, 5-(2-carboxyoctahydro-1H-indol-1-yl)-N-[N2-(2-naphthalenylcarbonyl)-L-lysyl]-5-oxo-, [2S-(2.alpha.,3a.beta.,7a.beta.)]-(9CI) (CA INDEX NAME)

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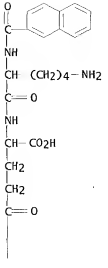

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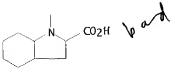

RN 128595-17-5 CAPLUS
CN D-Norvaline, 5-(2-carboxyoctahydro-1H-indol-1-yl)-N-[N2-(1-naphthalenylcarbonyl)-L-lysyl]-5-oxo-, [2S-(2.alpha.,3a.beta.,7a.beta.)]-(9CI) (CA INDEX NAME)

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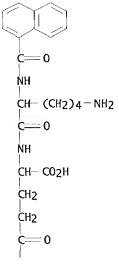
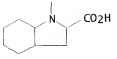
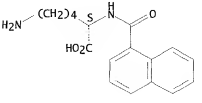




L91 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:406799 CAPLUS
DOCUMENT NUMBER: 113:6799
TITLE: Molecular design of inverted-aspartame-type sweeteners
AUTHOR(S): Nosho, Yasuharu; Seki, Takashi; Kondo, Miyuki; Ohfuji, Takehiko; Tamura, Masahiro; Okai, Hideo
CORPORATE SOURCE: Fac. Eng., Hiroshima Univ., Higashi-Hiroshima, 724, Japan
SOURCE: Journal of Agricultural and Food Chemistry (1990), 38(6), 1368-73
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of inverted aspartame-type sweeteners, e.g. PhCO(CH2)n-X-Lys-OH (I; n = 0-2; X = bond, Gly, .beta.-Ala, Ala, NHCH2CH2CO, NHCHEtCO) were prepd. and tested for sweetness potency. I (n = 1, X = Gly) was 50 times as sweet as sucrose. These sweeteners are useful because the lack of ester functions increases stability in soln. and lowers toxicity.
IT **126327-80-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sweetness of)
RN 126327-80-8 CAPLUS
CN L-Lysine, N2-(1-naphthalenylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:94921 CAPLUS
DOCUMENT NUMBER: 108:94921
TITLE: Amino acids and peptides. XVII. Synthesis of a tridecapeptide corresponding to the sequence 165-177 of T-kininogen (tryptic peptide) containing Gln-Val-Val-Ala-Gly sequence and the relationship between structure and effect on thiol proteinase
AUTHOR(S): Teno, Naoki; Tsuboi, Satoshi; Okada, Yoshio; Itoh, Norio; Okamoto, Hiroshi
CORPORATE SOURCE: Fac. Pharm. Sci., Kobe-Gakuin Univ., Kobe, 673, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1987), 35(9), 3853-8
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:94921
GI

H-Ser-Ala-His-Ser-Gln-Val-Val-
Ala-Gly-Met-Asn-Tyr-Lys-OH I

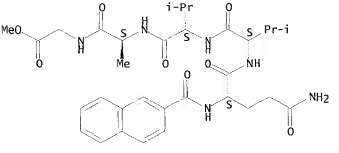
AB The title tridecapeptide I was prepd. by conventional soln. methods. Although Z-Gln-Val-Val-Ala-Gly-OMe showed inhibitory activity towards papain and protective activity against T-kininogen-induced inhibition of papain, the tryptic peptide obtained did not exhibit any effect on thiol proteinase. In order to study the relationship between structure and effect on thiol proteinase, R-Gln-Val-Val-Ala-Gly-OMe (II; R = Me3CO2C, H, Ac, Bz, .beta.-naphthoyl) were prepd. II (R = Bz, .beta.-naphthoyl) exhibited weak inhibitory and significant protective activities. A small peptide such as Gln-Val-Val-Ala-Gly might be better able to approach papain than I and the arom. ring assocd. with Gln-Val-Val-Ala-Gly at the N-terminus apparently strengthened the binding ability of the peptide to papain.

IT **112953-00-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and effect of, on papain)

RN 112953-00-1 CAPLUS

CN Glycine, N-[N-[N-[N-[N2-(2-naphthalenylcarbonyl)-L-glutaminyl]-L-valyl]-L-valyl]-L-alanyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:479373 CAPLUS
DOCUMENT NUMBER: 105:79373
TITLE: Histidine derivatives as renin inhibitors
INVENTOR(S): Iizuka, Kinji; Kamijo, Tetsuhide; Kubota, Tetsuhiro; Akahane, Kenji; Umeyama, Hideaki; Kiso, Yoshiaki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 108 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 181110	A2	19860514	EP 1985-307555	19851018 <--
EP 181110	A3	19880511		
R: BE, DE, FR, GB, IT, LU, NL, SE				
JP 61100595	A2	19860519	JP 1984-221853	19841022 <--
JP 05037422	B4	19930603		
JP 61137896	A2	19860625	JP 1984-260453	19841210 <--
JP 05037423	B4	19930603		
JP 61148167	A2	19860705	JP 1984-271303	19841222 <--
JP 05037424	B4	19930603		
US 4863904	A	19890905	US 1985-789597	19851021 <--

US 4656269	A	19870407	US 1986-852260	19860415 <--
US 4656269	B1	19890829	US 1988-90001688	19880110 <--

PRIORITY APPLN. INFO.:
JP 1984-221853 19841022
JP 1984-260453 19841210
JP 1984-271303 19841222
JP 1986-79726 19850415
US 1986-852260 19860415

OTHER SOURCE(S): CASREACT 105:79373

AB Histidine-contg. dipeptide derivs. are prepd. as proteinase-resistant renin inhibitors useful for oral treatment of renin-assocd. hypertension. For example, N-[2-(1-naphthylmethyl)-3-(phenethylcarbamoyl)propionyl]-L-histidyl-L-leucinal (I) (100 mg/kg orally) produced a 12-16% decrease in blood pressure within 2-3 h in high-renin (furosemide-treated) marmosets. To prep. I, 1-naphthaldehyde and Et succinate were condensed and converted in 2 steps to 2-(1-naphthylmethylene)succinic anhydride, condensed with phenethylamine to 2-(1-naphthylmethylene)-3-(phenethylcarbamoyl)propionic acid, hydrogenated over Pd/C, and the product was condensed with a L-histidyl-L-leucinal semicarbazone in the presence of diphenylphosphoryl azide.

IT **103633-13-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)

RN 103633-13-2 CAPLUS

CN L-Histidinamide, N-(1-naphthalenylacetyl)-2-(phenylmethyl)-.beta.-alanyl-N-[1-[[(aminocarbonyl)hydrazono]methyl]-3-methylbutyl]-, (S)- (9CI) (CA INDEX NAME)

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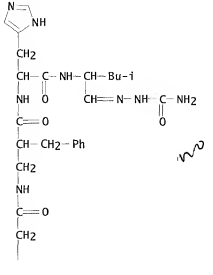

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